REMARKS

Applicants have received and reviewed the final Office Action dated November 5, 2003. In response, claims 5, 6, 19-39 and 41 have been canceled without prejudice, claims 1, 44, 47 and 48 have been amended, and new claim 49 has been added. Applicants submit that the pending claims are supported by the specification. Claims 1-4, 7-18, 40 and 42-49 remain in this application.

Claims 1, 44, and 48 have been amended to indicate that the basal medium in step b) is lacking the plant growth regulator having cytokinin activity. Support for the amendment may be found throughout the disclosure, for example, at page 22, Table 1, wherein a solid basal medium and a liquid basal medium are shown to lack cytokinin activity.

Claims 1 and 44 have been amended to indicate that the basal medium employed in the subculturing step is supplemented with at least one additive of interest. Support for the amendment may be found throughout the disclosure, for example, at page 29, last paragraph wherein the disclosure notes:

> In general terms, the method for the production of fortified phytopharmaceutical plants involves obtaining a sterile, rapidly growing plantlet, seedling or explant of a phytopharmaceutical plant and subculturing it on a medium supplemented with a nutrient mineral element.

Further support may be found in the Examples, particularly Examples 5 and 6, which describe phytofortification of *Echinacea* and St. John's wort with zinc and lithium, respectively. Specifically, the Examiner is directed to page 48, lines 1-3, wherein the disclosure indicates that:

> Mature seedlings were subcultured into 125 mL flasks containing 25 mL of basal medium supplemented with zinc...

and page 50, first full paragraph which discloses:

> The medium (liquid basal medium) was supplemented with lithium...

Claims 1 and 44 have also been amended to state that the method produces a phytopharmaceutical plant that is phytofortified.

Claim 47 has been amended to further clarify that the additive of interest is introduced in the step of subculturing (step c) of claim 1 and that the levels of the additive of interest in the plant as a result of the subculturing step are compared to that of a plant that is only grown in basal medium.

The preamble of claim 48 has also been amended to define a method for promoting shoot formation in a phytopharmaceutical plant. The subject matter pertaining to *in vitro* micropropagation involving *de novo* shoot formation of non-meristematic tissue of said phytopharmaceutical plant has been added to the end of the claim. By removing the subject matter from the preamble and placing it in the body of the claim, Applicant asserts that the subject matter is now considered a proper limitation of the claim.

New claim 49 has been added. It comprises the subject matter of old claim 41 rewritten in independent form including all the limitations of claim 1 from which claim 41 ultimately depended.

Applicant asserts that all of the amendments made to the claims are for the purpose of clarification.

For the reasons given below, Applicants submit that the amended claims are in condition for allowance and notification to that effect is earnestly solicited.

Claim Rejections Under 35 U.S.C. § 102

Claim 47 is rejected under 35 U.S.C. Section 102(b) as being anticipated by, or in the alternative under 35 U.S.C. Section 103(a) as obvious over Cellarova et al., as previously stated (paper 9, page 3). The previous Office Action (paper 9) asserted that:

> Cellarova et al. disclose a method for the in vitro propagation of a *Hypericum perforatum* plant on a medium comprising macroelements and microelements, 6-benzyladenine. This plant grown in medium comprising added macronutrients and micronutrient will contain a more elevated level of these nutrients than if grown on a basic medium. As a plant grown in soil contain more microelement than a plant grown in sterile water. The claim and Cellarova et al. state the same characteristics for the resultant *Hypericum perforatum* plant. Thus, the claimed invention as a whole was at least prima facie obvious over, if not anticipated by, the prior art.

Applicant disagrees with this assertion and respectfully traverses the rejection.

Cellarova discloses at page 267 (Section 2.2 Establishment of Tissue Cultures):

> For the initiation and culture of callus, the presence of exogenous auxins and cytokinins in the basal RM culture medium at ratios of 2:1 and 1:1, respectively, is required.

This disclosure indicates that plants are cultured on an induction medium comprising auxins and cytokinins in a ratio of 2:1 followed by culture of the callus in a culture medium comprising auxins and cytokinins in a ratio of 1:1. The presence of BAP in the RM culture medium is also stated at the top of page 268 (first full pararaph, second sentence). Thus, the subject matter disclosed by Cellarova teaches away from the method of the present invention by requiring cytokinin to be present in the initiation medium and the culture medium.

In contrast, claim 1 of the present application has been amended to clarify that the basal medium referred to in the step of transferring said regenerated tissue, and as defined on page 22, Table 1, lacks a plant growth regulator having cytokinin activity.

Applicant has also amended part (c) of claim 1 (upon which claim 47 depends) to clarify that the basal medium referred to in the step of subculturing is supplemented with at least one additive of interest, that the additive of interest is introduced in the step of subculturing (step c of claim 1), and that the levels of the additive of interest in the plant as a result of the subculturing step are compared to that of a plant that is only grown in basal medium. There is no disclosure or suggestion in Cellarova to employ a basal culture medium that is supplemented with at least one additive of interest.

The Office Action states that Cellerova grow plants in the presence of Ca and Zn, and that the levels of these additives would be elevated when compared to plants "grown on a basic medium". In response, Applicant notes that Cellerova teaches the growth of plants in a basal RM medium (v. a basic medium, suggested by Examiner). In the last sentence of page 267 it is stated that this "basal medium contains macroelements and microelements (according to Linsmaier and Skoog 1965)". We understand that the basal RM medium will contain Ca and Zn. However, Cellerova does not teach, or suggest, the

supplementing of the basal medium with one or more additional additives of interest, and comparing the levels of the additive of interest in the plant grown in the supplemented basal medium with those grown in the basal medium that lacks any supplement.

Claim 47 clearly states that the two plants are grown using a basal medium, and that one of the basal media is supplemented with an additive of interest. Examiners attention is directed to page 22, table 1 of the specification where the composition of the basal medium is disclosed. This basal medium comprises MS salts, including micro and macro elements and B5 vitamins in a similar manner to the basal medium of Cellerova. Therefore, any plant grown on the basal medium will have similar levels of macro and microelements, including Ca and Zn. However, the plant of claim 47 is produced using a basal medium that is supplemented with an additive, and the level of the additive in the plant grown using the supplemented medium when compared with the level of additive grown on a basal medium (in the absence of the additive), will be at an elevated level. Applicant submits that this is not analogous to comparing a plant grown in soil with one that is grown in distilled water as suggest by Examiner, as neither of these substrates (soil or distilled water) comprise a basal medium as stated in claim 1.

Based on the substantial differences between the subject matter claimed in the instant application and the Cellarova prior art document, Applicant asserts claim 47 of the present application is not disclosed or suggested by Cellarova. Removal of the objection under 35 U.S.C. 102(b), and/or 35 U.S.C. Section 103(a) is requested.

Claim Rejections – 35 U.S.C. § 103

Claims 1-18, 40, and 42-48 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Stojakowska et al., in view of Murthy et al., and further in view of Cellarova et al., as previously stated (paper 9, page 3). Applicant respectfully traverses the rejection.

Examiner states, in the paragraph spanning page 3-4 of the Office Action that in Stojakowska, a liquid MS medium comprising microelements such as Fe, Cu, Mn, Zn, etc. was used and that these additives are taken up by the plant. As noted above, these microelements are also present in the induction and basal media used in the present

invention. However, in Stojakowska these elements are not added over and above what is already present in the media being used. This is to be contrasted to the step of subculturing (step c)) in claim 1. The step of subculturing in claim 1 (and independent claims 44, 48 and new claim 49) specifies the use of a basal medium that already comprises macro and microelements (see Table 1, page 22), and states that the basal medium is supplemented with at least one additive of interest to produce a pytofortified phytopharmaceutical plant. Applicant submits that there is no disclosure or suggestion in any of the methods used in Stojakowska of supplementing the basal medium with one or more additives of interest. Stojakowska discloses the accumulation of parthenolide content that arises as a result of transforming a plant with an *Agrobacterium* (see page 161, RHC, first full para.). Parthenolide was not added to the basal medium as required in the step of subculturing (step c)) of claims 1, 44, 48 or 49 of the present application, and one of skill in the art would not have been lead to the method as defined in claim 1 upon reading of Stojakowska.

For the purposes of clarity, claims 1 and 44 have been amended so that the last step of the method now recites that a phytopharmaceutical plant that is phytofortified is produced. Applicant submits that Stojakowska do not disclose or suggest the production of a phytofortified phytopharmaceutical plant.

Murthy discloses the use of thidiazuron (TDZ) during plant culture. It is noted on page 273 (under the section "TDZ And Stress") that the addition of TDZ results in the accumulation of several mineral ions and other stress-related metabolites. The Office Action suggests that Applicant argued in their first response that Murphy do not teach the accumulation of mineral ions due to TDZ. Applicant respectfully disagrees with this conclusion, as no such statement is found in Applicant's earlier response.

Furthermore, Examiner states that Applicant argues that TDZ is not used in the medium employed. Again Applicant respectfully disagrees with Examiners conclusion. Applicant stated on page 12 (1st full para.) in their earlier response that:

> For example, the presently claimed subculturing (e.g. step (c) of claim 1), which is when the additive of interest is provided to the plant does not recite thidiazuron.

The step of subculturing in claim 1 (and independent claims 44, 48 and 49) involves the use of a basal medium. Reference to Table 1, on page 22 indicates that the basal medium is free of grow regulators, and therefore that TDZ is not present in the step of subculturing. However, TDZ may be used in the induction medium in the step of culturing (step a of claim1) as stated on page 20, last line of the page and as defined in claims 7 and 8.

Furthermore, Murthy do not disclose or suggest transferring regenerated tissue to a basal medium lacking a plant growth regulator or subculturing plantlets and supplementing the basal medium with at least one additive of interest as stated in claims 1, 44 48 and 49.

Applicant submits that there is no disclosure or suggestion in Murthy that would lead a person of skill in the art to the method as claimed in claim 1 of the present application.

Applicant also submits that the combined subject matter from Stojakowska and Murthy does not disclose or suggest any of the subject matter contained in the instant application.

In respect of the Cellarova reference, as noted above, this document does not disclose or suggest the subculturing of a plantlet on a basal medium that is free of growth regulators. Rather, Cellerova teaches away from the method of the present invention in that for the initiation and culture of callus, the presence of auxins and cytokinins in the basal RM culture medium must be in ratios of 2:1 and 1:1, respectfully. This reference specifically requires the culture media to comprise both auxins and cytokinins. Furthermore, there is no teaching or disclosure of a step comprising transferring regenerated tissue to a basal medium lacking a plant growth regulator having cytokinin activity and culturing to form plantlets. Further, Cellarova does not teach or disclose a basal medium which is supplemented with at least one additive of interest, nor subculturing plantlets on such a medium to allow uptake and accumulation of the at least one additive of interest in a bioavailable form.

Applicant notes that claims 2-18, 40, 42 and 43 all depend from claim 1 and claim 45-47 depend from claim 44, and that these dependent claims include the limitations of

claim 1 and 44. Claims 1, 44 and 48 each define that the step of subculturing involving the use of a basal medium that lacks a growth regulator having cytokinin activity. It is therefore submitted that claims 1-18, 40 and 42-48 claimed in the present application are not disclosed or suggested in Stojakowska et al., in view of Murthy et al., and Cellarova, et al., and removal of the objection under 35 U.S.C. 103(a) is requested.

SUMMARY

It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims are respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,
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